5. 510(k) Summary

Traditional Premarket Notification Submission (510(k)) Summary

Prepared in accordance with 21 CFR 807.92

5.1 Submitter Information

Sponsor name:	Dako North America, Inc.
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Sponsor Telephone:	805-566-6655
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Establishment Registration:	2022180
Contact person:	Jennifer Michelle Chambers MPA, MBA, CQA (ASQ)
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Date Summary Prepared:	March 22, 2013

5.2 Device Name

Trade (proprietary):	FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use, (Link)
Common (usual):	Anti-PR, Clone PgR 636
Classification:	21 CFR 864.1860: Immunohistochemistry (IHC) Reagents and Kits (Class II)
FDA Device Code:	MXZ: Immunohistochemistry Assay, Antibody, Progesterone Receptor
Panel:	88 (Pathology)

5.3 Substantially Equivalent Predicate Device

Device Name:	PR component of the Dako ER/PR pharmDx™ Kit
Device 510(k):	K042884

Table 3. Agreement between Anti-PR, Clone PgR 636 (ASCO/CAP) and Anti-PR Component of ER/PR pharmDx™ Kit (ASCO/CAP)

		Anti-PR Component of ER/PR pharmDx™ Kit		
		Positive	**Negative**	Total
Anti-PR, Clone PgR 636	**Positive**	115	8	123
	Negative	1	112	113
	Total	116	120	236

Positive Percent Agreement = 99.1% (95% CI: 93.0-98.0)
Negative Percent Agreement = 93.3% (95% CI: 92.8-98.0)
Overall Percent Agreement = 96.2% (95% CI: 93.0-98.0)

Table 4. Site 1 vs. Site 2 Inter Laboratory Reproducibility of Anti-PR, Clone PgR 636

		Site 1		
		Positive	**Negative**	Total
Site 2	**Positive**	55	0	55
	Negative	4	46	50
	Total	59	46	105

Average Positive Percent Agreement = 96.5%
Average Negative Percent Agreement = 95.8%

Table 5. Site 1 vs. Site 3 Inter Laboratory Reproducibility of Anti-PR, Clone PgR 636

		Site 1		
		Positive	**Negative**	Total
Site 3	**Positive**	59	1	60
	Negative	0	45	45
	Total	59	46	105

Average Positive Percent Agreement = 99.2%
Average Negative Percent Agreement = 98.9%

Table 6. Site 2 vs. Site 3 Inter Laboratory Reproducibility of Anti-PR, Clone PgR 636

		Site 2		
		Positive	**Negative**	Total
Site 3	**Positive**	55	5	60
	Negative	0	45	45
	Total	55	50	105

Average Positive Percent Agreement = 95.7%
Average Negative Percent Agreement = 94.7%

5.4 Device Description

Dako FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use, (Link) antibody is utilized to semi-quantitatively detect human progesterone receptor in formalin-fixed, paraffin-embedded (FFPE) human breast carcinoma. This product is pre-diluted and optimized for use with the Dako Autostainer Link 48 automated slide staining platform. Anti-PR, Clone PgR 636 is provided in liquid form in a buffer containing stabilizing protein and 0.015 mol/L sodium azide. The target concentration of Anti-PR, Clone PgR 636 is 0.5 µg/mL; the acceptable concentration range is 0.4 µg/mL to 0.6 µg/mL.

5.5 Intended Use

For in vitro diagnostic use.

FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-use (Link) is intended for use in immunohistochemistry with EnVision™ FLEX+, High pH visualization kit together with Autostainer Link 48 instrument to semi-quantitatively detect human progesterone receptor in formalin-fixed, paraffin-embedded (FFPE) human breast carcinoma. This antibody labels progesterone receptor-positive cells and is useful in the assessment of progesterone receptor status in human breast carcinomas.

The clinical interpretation of any staining or its absence should be complemented by morphological studies using proper controls and should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.

5.6 Technological Characteristics

Dako FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-use (Link) Antibody IHC assay and the predicate PR component of the Dako ER/PR pharmDx™ Kit both specifically bind to PR proteins located in the cell nucleus of PR-expressing cells, and are optimized for use on formalin-fixed, paraffin-embedded (FFPE) tissues. Both products aid in the prognosis of breast carcinoma, both products have equivalent staining performance, and both products require similar detection chemistry principles for visualization of the product. The difference in visualization between the predicate device and Anti-PR, Clone PgR 636 has been clinically validated to ensure it does not introduce new issues of safety or effectiveness.

5.7 Performance Characteristics (Nonclinical)

Nonclinical Performance characteristics evaluated in support of the FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-use (Link) Antibody IHC assay include analytical specificity and precision. Study results demonstrate a substantial degree of equivalency to the predicate device.

5.8 Performance Characteristics (Clinical)

Clinical Performance characteristics evaluated in support of the FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-use (Link) Antibody IHC assay include concordance and reproducibility. Summaries of all performance testing are provided in the Executive Summary of this 510(k). Full reports of all performance testing are provided in the Performance Testing (Clinical) section of this 510(k).

Concordance: Anti-PR, Clone PgR 636 testing was performed with EnVision™ FLEX+ and scored according to ASCO/CAP guidelines (≥1% cut-off) (11). Anti-PR (Clone 1294) testing was performed using Dako ER/PR pharmDx™ Kit and scored using the Allred scoring guideline described in the package insert. The method comparison data are presented (Table 2). Using these respective scoring guidelines, Anti-PR, Clone PgR 636 was concordant with the PR antibody component of Dako ER/PR pharmDx™ Kit, exhibiting values for overall, positive and negative agreement of 94.5%, 95.8% and 93.1%, respectively. Both assays were compared when scored using the ASCO/CAP guidelines (Table 3). Study results demonstrate a substantial degree of equivalency to the predicate device.

Reproducibility: Anti-PR, Clone PgR 636 reproducibility testing was performed in three testing laboratories over five non-consecutive days on 21 unique breast cancer specimens, and scored according to ASCO/CAP guidelines (≥1% cut-off) for a total of 315 evaluations. Site to site reproducibility of the assay is detailed (Table 4, Table 5, and Table 6). The average positive and average negative percent agreement calculations support the highly reproducible results of the PR (PgR 636) assay when used for the determination of PR status in a clinical setting.

Table 2. Agreement between Anti-PR, Clone PgR 636 (ASCO/CAP) and Anti-PR Component of ER/PR pharmDx™ Kit (Allred)

		Anti-PR Component of ER/PR pharmDx™ Kit		
		Positive	**Negative**	Total
Anti-PR, Clone PgR 636	**Positive**	115	8	123
	Negative	5	108	113
	Total	120	116	236

Positive Percent Agreement = 95.8% (95% CI: 91.1-96.8)
Negative Percent Agreement = 93.1% (95% CI: 90.5-96.7)
Overall Percent Agreement = 94.5% (95% CI: 90.8-96.8)

Analytical specificity: Anti-PR, Clone PgR 636 immunoreactivity was tested on the recommended panel of normal tissues (Table 1). All tissues were formalin-fixed, paraffin-embedded, and stained with Anti- PR, Clone PgR 636 according to the instructions in the package insert. Cytoplasmic staining was observed with Anti-PR, Clone PgR 636 in several different tissue elements including epithelium, stroma, interstitial cells and inflammatory cells. While cytoplasmic staining was observed, it is not considered diagnostic per the intended use of this antibody.

Precision: Serial sections from each of 12 different FFPE blocks of breast carcinoma, representing a dynamic range of PR expression, were collected for testing. Testing was performed as follows:

Intra-run precision: Following the standard EnVision™ FLEX+, High pH protocol, three sections from each tissue block were stained with Anti-PR, Clone PgR 636. Concurrently, one section from each block was stained with a negative control reagent.

Inter-run precision: Staining one section from each tissue block, the above procedure was repeated on five non-consecutive days. Concurrently, one section from each tissue block was stained with a negative control reagent.

Inter-instrument precision: Staining a total of three sections from each tissue block, the above procedure was performed on three different Autostainer instruments by three different operators. Concurrently, one slide from each tissue block was stained with a negative control reagent.

Precision experiments with Anti-PR, Clone PgR 636 yielded consistent results with intra-run, inter-run and inter-instrument testing. Consistent test conditions were maintained throughout the study, and reagents were stored at 2-8 °C between test runs.

Table 1. Summary of Anti-PR, Clone PgR 636 Normal Tissue Reactivity

Tissue Type (# tested)	Positive Tissue Elements
Adrenal (3)	1/3 cells in glomerulosa region (50%), nuclear
	1/3 cells in glomerulosa region (50%), nuclear
Bone marrow (3)	0/3
Breast (3)	2/3 Glandular epithelial cells (50-90%), nuclear
Cerebellum (3)	0/3
Cerebrum (3)	1/3 Meningial cells (100%), nuclear
Cervix (3)	3/3 Epithelial cells (50-90%), nuclear
	3/3 Stroma, including inflammatory cells (50%), nuclear
Colon (3)	1/3 Lymphoid/inflammatory cells (10%), nuclear
	1/3 Lympoid/inflammatory cells (10%), nuclear
Esophagus (3)	1/3 Stromal cells (50%), nuclear
Kidney (3)	3/3 Interstitial cells (1-5%), nuclear
Liver (3)	0/3
Lung (3)	2/3 Interstitial cells (1-10%), nuclear
	2/3 Inflammatory cells (1-10%), nuclear
Mesothelial cells (2)	0/2
Muscle, cardiac (3)	3/3 Myocytes (30%), peri-nuclear
Muscle, skeletal (3)	0/3
Nerve, peripheral (3)	0/3
Ovary (3)	3/3 Stromal cells (50-70%), nuclear
Pancreas (3)	2/3 Islets of Langerhans (50-90%), nuclear
Parathyroid (3)	3/3 Glandular epithelial cells (1-10%), nuclear
Pituitary (3)	3/3 Pituitary glandular cells (1-40%), nuclear
Prostate (3)	3/3 Stromal cells (30-80%), nuclear
Salivary gland (3)	3/3 Glandular epithelial cells (<1%-60%), nuclear
Skin (3)	0/3
Small intestine (3)	3/3 Stromal and inflammatory cells (30-50%), nuclear
Spleen (3)	0/3
Stomach (3)	1/3 Interstitial cells (20%), nuclear
Testis (3)	3/3 Interstitial cells (5-80%), nuclear
Thymus (3)	0/3
Thyroid (3)	0/3
Tonsil (3)	0/3
Uterus (2)	2/2 Glandular epithelial cells (100%), nuclear 2/2 Myometrial stromal cells (100%), nuclear

In addition to the testing referenced above, additional nonclinical studies in support of the substantial equivalence of Anti-PR, Clone PgR 636 include lot-to-lot and stability testing. An additional study is referenced: Analytical sensitivity for antibody characterization, established for PgR 636 concentrate in K020023. Summaries of all performance testing are provided in the Executive Summary of this 510(k). Full reports of all performance testing are provided in the Performance Testing (Bench) section of this 510(k).

5.9 Conclusion

Based on the information provided in this premarket notification, Dako concludes that the FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-use (Link) Antibody IHC assay is safe, effective, and substantially equivalent to the predicate device PR component of the Dako ER/PR pharmDx™ Kit in its indication for use, device design, materials, performance characteristics, and operational principles.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

December 9, 2013

Dako North America, Inc
Jennifer Michelle Chambers
6392 Via Real
Carpinteria, CA 93013

Re: K130861
Trade/Device Name: Dako FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use, (Link)
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: II
Product Code: MXZ
Dated: November 8, 2013
Received: November 12, 2013

Dear Ms. Chambers:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Reena Philip -S

for

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and
Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130861

Device Name
FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use, (Link)

Indications for Use *(Describe)*
For in vitro diagnostic use.

FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use, (LINK) is intended for use in immunohistochemistry with EnVision™ FLEX +, High pH visualization kit together with the Autostainer Link 48 instrument to semiquantitatively detect human progesterone receptor in formalin fixed, paraffin embedded human breast carcinoma. This antibody labels progesterone receptor positive cells and is useful in the assessment of progesterone receptor status in human breast carcinomas.

The clinical interpretation of any staining or its absence should be complemented by morphological studies using proper controls and should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Reena Philip -S